DOCKET NO: 285327US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
YUKIHIKO SAEKI, ET AL.	: EXAMINER: RAE, C. E.
SERIAL NO: 10/566,253	:
FILED: JANUARY 30, 2006	: GROUP ART UNIT: 1611
FOR: METHOD OF INHIBITING PRODUCTION OF OSTEOPONTIN	:

REPLY BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

The following Reply Brief is in reply to the Examiner's Answer dated November 28, 2008 (Answer).

Applicants acknowledge that the Examiner has withdrawn the rejection, as stated under Ground (C) in the Appeal Brief, and that Claim 34 is no longer subject to the rejection stated under Ground (A) of the Appeal Brief (Answer at 2).

The Examiner finds that Applicants have stated Grounds (A) and (B) incorrectly in the Appeal Brief in that, according to the Examiner, WO 00/63241 (Ashkar et al) was incorrectly listed in the statement of the rejection (Answer at 2-3). The Examiner finds that Ashkar et al "is only relied upon as an evidentiary reference", and therefore, the *Hoch* case, cited in the Appeal Brief at 5 n.1 , does not apply (Answer at 3 and 7).

In reply, the Examiner's finding raises form over substance. **Every** reference relied on in **any** rejection is an *evidentiary reference*, since it is the evidence relied on by the

Examiner to support the rejection. The result in this appeal is the same regardless of how the Examiner states the rejections, since Ashkar et al is still relied on to support the rejections.

With regard to the merits of the rejections under Ground (A) and Ground (B), Applicants have essentially responded to the statement of these rejections (Answer at 4-7) in the Appeal Brief. The remainder of this Reply Brief is in reply to the "Response to Argument" (Answer at 7-12).

The Examiner continues to ignore the fact that while some kidney diseases are associated with enhanced OPN production, which diseases are covered by the present claims, the Examiner has not established that **any** kidney disease is so associated, and particularly with regard to ischemic nephritis, which is a kidney disease disclosed by Ohkuchi et al that is caused by stimulation of interleukin-1β production (column 13, line 10ff). Note that present Claim 33 recites, *inter alia*, "**a** kidney disease" (emphasis added), not kidney disease or kidney diseases. The Examiner's rationale is analogous to rejecting a claim drawn to the treatment of stomach cancer over a prior art reference disclosing treatment of gastroenteritis, since stomach cancer and gastroenteritis are both stomach diseases. The only kidney diseases within the terms of the present claims are those resulting from enhanced OPN production, not any kidney disease.

The Examiner finds that Applicants' argument that it has not been shown that ischemic nephritis is associated with enhanced OPN production "is inconsistent (emphasis by the Examiner) with the instant application wherein it is expressly stated that 'OPN production is known to be increased in kidney disease.' See specification, page 2, para. 0003. Thus, the teaching of ischemic nephritis by [Ohkuchi et al] provides a nexus between IL-1 beta and osteopontin as evidenced by [Ashkar et al]" (Answer at 9).

In reply, the reference to kidney disease in the specification at paragraph [0003] (page 2, lines 5-6) cites a so-called "Non-patent Document 2", the citation of which is disclosed in

the specification at page 3, lines 7-8 (Gauer et al). Gauer et al is of record in the present application, as it was filed as part of an Information Disclosure Statement (IDS) on November 28, 2006. This reference discloses nothing with regard to ischemic nephritis and does not disclose or suggest that all kidney diseases are associated with enhanced OPN production. Applicants maintain that the Examiner has not shown a nexus between interleukin-1β production and OPN production. It follows that the Examiner has not met his burden to show any overlap in the respective universe of populations in need of the recited pyridazine derivative. With regard to the substantive disclosure of Ashkar et al, Applicants maintain the arguments with respect thereto in the Appeal Brief.

With regard to McPhaden et al, it states, *inter alia*, "[a] number of osteoclast activating factors have been implicated in multiple myeloma including IL-6, IL-1β, TNF and TGFβ. One or more of these factors may upregulate OPN production from osteoblasts or osteoclasts. Further study is needed to clarify the source and regulation of OPN in myeloma patients. Our results suggest that plasma OPN may be a useful clinical marker for disease severity in multiple myeloma. Perspective longitudinal studies will be necessary to test this hypothesis." Thus, McPhaden et al does not disclose or suggest to persons of ordinary skill in the art that a compound that inhibits interleukin-1β production will be useful in treating a disease resulting from enhanced OPN production.

For all the above reasons, it is respectfully requested that the rejections under Ground (A) and Ground (B) be REVERSED.

Respectfully submitted,

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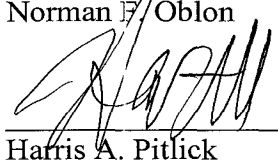
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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